



## Supporting Information

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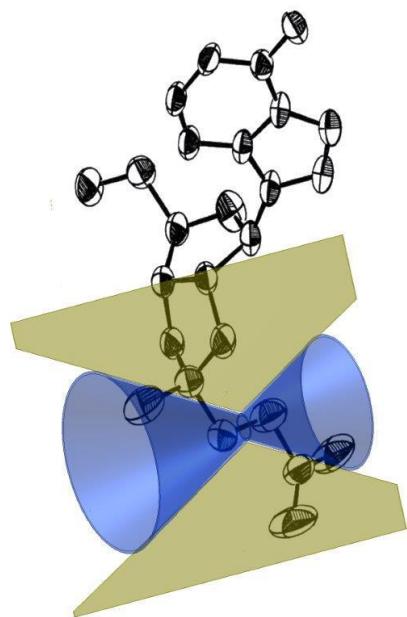
### Nucleolipids of Canonical Purine $\beta$ -D-Ribo-Nucleosides: Synthesis and Cytostatic/Cytotoxic Activities Toward Human and Rat Glioblastoma Cells

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## Supporting Information

**Figure S1.** Positive shielding (grey) of glyconic carbon resonances ((C(2'), C(3')) by the magnetic anisotropy effect of a C-C single bond {CH<sub>2</sub>(acetal) – CH<sub>2</sub>(C=O)} within (1*R*)-O-2',3'-[1-(2-carboxyethyl)ethyliden]adenosine<sup>[14]</sup>, the saponification product of compound 3. Negative shielding occurs within the blue-colored double cone.



## Chemistry

**Ethyl 3-[4-(6-amino-purin-9-yl)-6-hydroxymethyl-2-methyl-tetrahydro-furo[3,4-*d*][1,3]dioxol-2-yl]-propionate (3, NL\_5.1.0.0, <sup>[8]</sup>, diastereoisomeric mixture).** Mp. 154.5 °C. TLC (SiO<sub>2</sub> 60): *R*<sub>f</sub> (SiO<sub>2</sub> 60, CH<sub>2</sub>Cl<sub>2</sub>/Methanol, [MeOH 9:1]) = 0.38. UV (MeOH): 259 (16.020). log *P*<sub>ow</sub> ( ALOGPS 3.01): 0.87 ± 0.74. <sup>1</sup>H-NMR [D<sub>6</sub>]DMSO; (1*R*)-NL\_5.1.0.0 diastereoisomer): 8.383 (s, H-C(2)); 8.212 (s, H-C(8)); 7.421 (s, NH<sub>2</sub>); 6.173 (d, *J*(1',2') = 2.5, H-C(1')); 5.448 (*dd*, <sup>3</sup>*J*(2',1') = 2.5, *J*(2',3') = 6.3, H-C(2')); 5.110 (*t*, *J*(HO-C(5'),5') = 5.4, HO-C(5')); 5.00 (*dd*, *J*(3',2') = 6.5, *J*(3',4') = 2.4, H-C(3')); 4.244 (*Ψq*, *J*(4',3') = 2.5, *J*(4',5') = 5.0, H-C(4')); 4.09 (q,

$J(\text{CH}_2(\text{ester}), \text{Me}(\text{ester})) = 7.1$ ,  $\text{CH}_2(\text{ester})$ ; 3.55-3.46 ( $m$ ,  $\text{CH}_2(5')$ ); 2.499 ( $t$ ,  $J(\text{CH}_2(\text{C=O}), \text{CH}_2(\text{acetal})) = 7.6$ ,  $\text{CH}_2(\text{C=O})$ ); 2.108 ( $t$ ,  $J(\text{CH}_2(\text{acetal}), \text{CH}_2(\text{C=O})) = 7.7$ ,  $\text{CH}_2(\text{acetal})$ ); 1.335 ( $s$ ,  $\text{Me}(\text{acetal})$ ); 1.225 ( $t$ ,  $J(\text{Me}(\text{ester}), \text{CH}_2(\text{ester})) = 7.1$ ,  $\text{Me}(\text{ester})$ ).  $^1\text{H-NMR}$  ((D<sub>6</sub>)DMSO); (1S)-diastereoisomer (only selected resonances which are different from those of the (1R)-NL\_5.1.0.0 diastereoisomer [23]): 4.047 ( $q$ ,  $J(\text{CH}_2(\text{ester}), \text{Me}(\text{ester})) = 7.0$ ,  $\text{CH}_2(\text{ester})$ ); 2.343 ( $t$ ,  $J(\text{CH}_2(\text{C=O}), \text{CH}_2(\text{acetal})) = 7.6$ ,  $\text{CH}_2(\text{C=O})$ ); 1.933 ( $t$ ,  $J(\text{CH}_2(\text{acetal}), \text{CH}_2(\text{C=O})) = 7.7$ ,  $\text{CH}_2(\text{acetal})$ ); 1.532 ( $s$ ,  $\text{Me}(\text{acetal})$ ); 1.161 ( $t$ ,  $J(\text{Me}(\text{ester}), \text{CH}_2(\text{ester})) = 7.0$ ,  $\text{Me}(\text{ester})$ ).  $^{13}\text{C-NMR}$  ((D<sub>6</sub>)DMSO); (1R)-NL\_5.1.0.0 diastereoisomer): 172.521 (C=O(ester)); 156.787 (C(6)); 152.226 (C(2)); 148.774 (C(4)); 139.754 (C(8)); 119.010 (C(5)); 113.732 (C(acetal)); 89.400 (C(1')); 86.576 (C(4')); 83.391 (C(2')); 81.296 (C(3')); 61.428 (C(5')); 59.846 (CH<sub>2</sub>(ester)); 33.434 (CH<sub>2</sub>(C=O)); 28.155 (CH<sub>2</sub>(acetal)); 23.467 (Me(acetal)); 13.992 (Me(ester)).  $^{13}\text{C-NMR}$  [D<sub>6</sub>]DMSO; (1S)-NL\_5.1.0.0 diastereoisomer) (only selected resonances which are different from those of the (1R)-NL\_5.1.0.0 diastereoisomer): 172.391 (C=O(ester)); 139.804 (C(8)); 114.114 (C(acetal)); 89.660 (C(1')); 86.735 (C(4')); 83.824 (C(2')); 81.831 (C(3')); 61.514 (C(5')); 59.788 (CH<sub>2</sub>(ester)); 33.282 (CH<sub>2</sub>(C=O)); 28.956 (CH<sub>2</sub>(acetal)); 24.868 (Me(acetal)); 13.912 (Me(ester)). HR-ESI-MS: 394.18 ([M+H]<sup>+</sup>); (calc. 393.39). Anal. calc. for C<sub>17</sub>H<sub>23</sub>N<sub>5</sub>O<sub>6</sub> (393.39): C 51.90, H 5.89, N 17.80. Found: C 51.94, H 5.86, N 17.91.

**Ethyl 3-[4-hydroxymethyl-2-methyl-6-(6-oxo-1,6-dihydro-purin-9-yl)-tetrahydro-furo[3,4-d][1,3]dioxol-2-yl]-propionate (4, NL\_6.1.0.0)** [9, 11, 23]. A) By Enzymatic Deamination of Compound 3: Mp: 202.5 °C. TLC (SiO<sub>2</sub> 60, CH<sub>2</sub>Cl<sub>2</sub>/MeOH 9:1): R<sub>f</sub> 0.41. UV (MeOH): 249 (10.300). logP<sub>ow</sub> (ALOGPS 3.01): -0.08 ± 0.74.  $^1\text{H-NMR}$

((D<sub>6</sub>)DMSO); (1*R*)-NL\_6.1.0.0, [23]): 11.28 (s, H-N(1)); 8.27 (s, H-C(2)); 8.07 (s, H-C(8)); 6.11 (d, <sup>3</sup>J(1',2') = 2.5, H-C(1')); 5.34 (dd, <sup>3</sup>J(2',1') = 2.7, <sup>3</sup>J(2',3') = 6.5, H-C(2')); 5.05 (s, HO-C(5')); 4.96 (dd, <sup>3</sup>J(3',2') = 6.6, <sup>3</sup>J(3',4') = 2.2, H-C(3')); 4.21 (m, H-C(4')); 4.08 (q, <sup>3</sup>J(CH<sub>2</sub>(ester),Me(ester)) = 6.9, CH<sub>2</sub>(ester)); 3.51 (d, <sup>3</sup>J(5',HO-C(5')) = 4.1, CH<sub>2</sub>(5')); 2.46 (t, <sup>3</sup>J(CH<sub>2</sub>(C=O),CH<sub>2</sub>(acetal)) = 7.6, CH<sub>2</sub>(C=O)); 2.07 (t, <sup>3</sup>J(CH<sub>2</sub>(acetal),CH<sub>2</sub>(C=O)) = 7.6, CH<sub>2</sub>(acetal)); 1.30 (s, Me(acetal)); 1.20 (t, <sup>3</sup>J(Me(ester),CH<sub>2</sub>(ester)) = 7.1, Me(ester)). <sup>13</sup>C-NMR ((D<sub>6</sub>)DMSO); (1*R*) NL\_6.1.0.0): 172.46 (C=O(ester)); 156.49 (C(6)); 147.68 (C(2)); 145.97 (C(4)); 138.59 (C(8)); 124.41 (C(5)); 113.74 (C(acetal)); 89.32 (C(1')); 86.69 (C(4')); 83.78 (C(3')); 81.14 (C(2')); 61.30 (C(5')); 59.81 (CH<sub>2</sub>(ester)); 33.33 (CH<sub>2</sub>(C=O)); 28.08 (CH<sub>2</sub>(acetal)); 23.44 (Me(acetal)); 13.97 (Me(ester)). HR-ESI-MS: 394.20 ([M+H]<sup>+</sup>); C<sub>17</sub>H<sub>22</sub>N<sub>4</sub>O<sub>7</sub> (394.38). Anal. calc. for C<sub>17</sub>H<sub>22</sub>N<sub>4</sub>O<sub>7</sub> (394.38): C 51.77, H 5.62, N 14.21. Found: C 51.70, H 5.55, N 14.20. B) *By Direct Ketal Formation of Inosine*: TLC (SiO<sub>2</sub> 60. CH<sub>2</sub>Cl<sub>2</sub>/MeOH; 85:15; v/v): R<sub>f</sub>, 0.56. The material proved to be identical with an authentic sample <sup>[9, 11]</sup> in all respects, except of the NMR data. <sup>1</sup>H-NMR ((D<sub>6</sub>)DMSO); (1*R*)-NL\_6.1.0.0): 12.379 (s, NH); 8.284 (s, H-C(2)); 8.076 (s, H-C(8)); 6.118 (d, <sup>3</sup>J(1',2') = 2.5, H-C(1'), (1*R*) + (1*S*)); 5.337 (dd, <sup>3</sup>J(2',1') = 2.5, <sup>3</sup>J(2',3') = 6.5, H-C(2')); 5.059 (t, <sup>3</sup>J(HO-C(5'),CH<sub>2</sub>(5')) = 5.5, HO-C(5')); 4.962 (dd, <sup>3</sup>J(3',2') = 6.5, <sup>3</sup>J(3',4') = 2.5, H-C(3')); 4.215 (td, <sup>3</sup>J(4',3') = 2.5, <sup>3</sup>J(4',CH<sub>2</sub>(5')) = 4.5, H-C(4')); 4.073 (q, <sup>3</sup>J(CH<sub>2</sub>(ester),Me(ester)) = 7.0, CH<sub>2</sub>(ester)); 3.521 – 3.503 (m, CH<sub>2</sub>(5'), (1*R*) + (1*S*)); 2.453 (t, <sup>3</sup>J(CH<sub>2</sub>(C=O),CH<sub>2</sub>(acetal)) = 7.5, CH<sub>2</sub>(C=O)); 2.069 (t, <sup>3</sup>J(CH<sub>2</sub>(acetal),CH<sub>2</sub>(C=O)) = 7.5, CH<sub>2</sub>(acetal)); 1.299 (s, Me(acetal)); 1.191 (t, <sup>3</sup>J(Me(ester),CH<sub>2</sub>(ester)) = 7.0, Me(ester)). <sup>1</sup>H-NMR ((D<sub>6</sub>)DMSO); (1*S*)-NL\_6.1.0.0 diastereoisomer (only selected resonances which are different from those of the (1*R*)-NL\_6.1.0.0 diastereoisomer): 5.274 (dd, <sup>3</sup>J(2',1') = 2.5, <sup>3</sup>J(2',3') = 6.5, H-C(2')); 4.943 (dd, <sup>3</sup>J(3',2') = 6.5, <sup>3</sup>J(3',4') = 2.5, H-C(3')); 4.021 (q, <sup>3</sup>J(CH<sub>2</sub>(ester),Me(ester)) = 7.0,

$\text{CH}_2(\text{ester})$ ); 2.307 ( $t$ ,  $^3J(\text{CH}_2(\text{C=O}), \text{CH}_2(\text{acetal})) = 7.5$ ,  $\text{CH}_2(\text{C=O})$ ); 1.895 ( $t$ ,  $^3J(\text{CH}_2(\text{acetal}), \text{CH}_2(\text{C=O})) = 7.5$ ,  $\text{CH}_2(\text{acetal})$ ); 1.136 ( $t$ ,  $^3J(\text{Me}(\text{ester}), \text{CH}_2(\text{ester})) = 7.0$ ,  $\text{Me}(\text{ester})$ ).  $^{13}\text{C}$ -NMR (( $D_6$ )DMSO); ( $1R$ ) NL\_6.1.0.0: 172.551 (C=O(ester)); 156.498 (C(6)), 147.763 (C(2)); 145.959 (C(4)); 138.728 (C(8)); 124.465 (C(acetal)); 89.415 (C(1’)); 86.800 (C(4’)); 83.890 (C(3’)); 81.212 (C(2’)); 61.387 (C(5’)); 69.904 ( $\text{CH}_2(\text{ester})$ ); 33.396 ( $\text{CH}_2(\text{C=O})$ ); 28.153 ( $\text{CH}_2(\text{acetal})$ ); 23.498 ( $\text{Me}(\text{acetal})$ ); 14.028 ( $\text{Me}(\text{ester})$ ).  $^{13}\text{C}$ -NMR (( $D_6$ )DMSO); ( $1S$ )-NL\_6.1.0.0 diastereoisomer (only selected resonances which are different from those of the ( $1R$ )-NL\_6.1.0.0 diastereoisomer): 172.435 (C=O(ester)); 138.793 (C(8)); 114.239 (C(acetal)); 89.639 (C(1’)); 86.953 (C(4’)); 84.326 (C(3’)); 81.732 (C(2’)); 61.450 (C(5’)); 59.853 ( $\text{CH}_2(\text{ester})$ ); 33.305 ( $\text{CH}_2(\text{C=O})$ ); 28.980 ( $\text{CH}_2(\text{acetal})$ ); 24.874 ( $\text{Me}(\text{acetal})$ ); 13.971 ( $\text{Me}(\text{ester})$ ).

**6-(6-Amino-purin-9-yl)-2,2-dinonyl-tetrahydro-furo[3,4-d][1,3]dioxol-4-yl]-methanol (5, NL\_5.3.0.0 [23]).** TLC ( $\text{SiO}_2$  60,  $\text{CHCl}_3/\text{EtOH}$  87:13):  $R_f$ , 0.56. UV (MeOH): 259 (13.100).  $^1\text{H}$ -NMR (( $D_6$ )DMSO): 8.331 (s, H-C(2)); 8.144 (s, H-C(8)); 7.277 (s,  $\text{NH}_2$ ); 6.131 (d,  $J(1',2') = 2.3$ , H-C(1’)); 5.358 (dd,  $J(2',1') = 2.2$ ,  $J(2',3') = 5.0$ , H-C(2’)); 5.099 (t,  $J(\text{HO-C}(5'),5') = 5.5$ , HO-C(5’)); 4.960 (d,  $J(3',2') = 5.0$ , H-C(3’)); 3.540 – 3.469 (m,  $\text{CH}_2(5')$ ); 1.720 ( $t$ ,  $J(\text{CH}_2(1''_{\text{endo}}), \text{CH}_2(2''_{\text{endo}})) = 7.5$ ,  $\text{CH}_2(1''_{\text{endo}})$ ); 1.556 ( $t$ ,  $J(\text{CH}_2(1''_{\text{exo}}), \text{CH}_2(2''_{\text{exo}})) = 7.5$ ,  $\text{CH}_2(1''_{\text{exo}})$ ); 1.424 ( $t$ ,  $J(\text{CH}_2(2''_{\text{endo}}), \text{CH}_2(1''_{\text{endo}})) = 7.5$ ,  $\text{CH}_2(2''_{\text{endo}})$ ); 1.298 – 1.129 (m,  $\text{CH}_2(2''_{\text{exo}})$ , 13 x ( $\text{CH}_2(\text{ketal})$ )); 0.871 – 0.824 (m, 2 x Me).  $^{13}\text{C}$ -NMR (( $D_6$ )DMSO): 156.026 (C(6)); 152.504 (C(2)); 148.788 (C(4)); 139.587 (C(8)); 118.961 (C(5)); 116.643 (C(acetal)); 89.396 (C(4’)); 86.802 (C(1’)); 83.515 (C(2’)); 81.448 (C(3’)); 61.501 (C(5’)); 36.348 ( $\text{C}_{\text{endo}}(1'')$ ); 36.119 ( $\text{C}_{\text{exo}}(1'')$ ); 31.174, 31.132, 29.019, 28.808, 28.740, 28.564, 28.523, 23.483, 22.870, 21.965, 21.931 (13  $\text{CH}_2(\text{ketal})$ ); 13.795, 13.767 (2  $\text{CH}_3$ ). HR-

ESI-MS: 532.34 [M+H]<sup>+</sup>; C<sub>29</sub>H<sub>49</sub>N<sub>5</sub>O<sub>4</sub> (531.38). Anal. calc. for C<sub>29</sub>H<sub>49</sub>N<sub>5</sub>O<sub>4</sub> (531.38 g/mol): C 65.51, H 9.29, N 13.17. Found: C 65.52, H 8.96, N 12.91.

**9-(6-Hydroxymethyl-2,2-dinonyl-tetrahydro-furo[3,4-d][1,3-dioxol-4-yl])-1,9-dihydro-purin-6-one (6, NL\_6.3.0.0).** TLC (SiO<sub>2</sub> 60, CH<sub>2</sub>Cl<sub>2</sub>/MeOH 9:1): R<sub>f</sub> 0.42. UV (MeOH): 248 (18.100). <sup>1</sup>H-NMR ((D<sub>6</sub>)DMSO): 12.367 (s, NH); 8.295 (s, H-C(2)); 8.057 (s, H-C(8)); 6.109 (d, J(1',2') = 2.2, H-C(1')); 5.282 (dd, J(2',1') = 2.0, J(2',3') = 6.0, H-C(2')); 5.027 (t, J(HO-C(5'),5') = 5.5, HO-C(5')); 4.932 ( $\Psi$ t, J(3',4') = 6.0, J(3',4') = 5.8, H-C(3')); 4.201 – 4.196 (m, H-C(4')); 3.520 – 3.500 (m, CH<sub>2</sub>(5')); 1.712 (t, J(CH<sub>2</sub>(1''<sub>endo</sub>),CH<sub>2</sub>(2''<sub>endo</sub>)) = 7.5, CH<sub>2</sub>(1''<sub>endo</sub>)); 1.550 (t, J(CH<sub>2</sub>(1''<sub>exo</sub>),CH<sub>2</sub>(2''<sub>exo</sub>)) = 7.5, CH<sub>2</sub>(1''<sub>exo</sub>)); 1.415 (t, J(CH<sub>2</sub>(2''<sub>endo</sub>),CH<sub>2</sub>(1''<sub>endo</sub>)) = 7.5, CH<sub>2</sub>(2''<sub>endo</sub>)); 1.290 – 1.229 (m, CH<sub>2</sub>(2''<sub>exo</sub>), 13 x CH<sub>2</sub>(ketal)); 0.842 – 0.825 (m, 2 x Me). <sup>13</sup>C-NMR ((D<sub>6</sub>)DMSO): 156.401 (C(6)); 147.709 (C(2)); 145.849 (C(4)); 138.702 (C(8)); 124.377 (C(5)); 116.699 (C(acetal)); 89.468 (C(4')); 87.070 (C(1')); 84.032 (C(2')); 81.385 (C(3')); 61.431 (C(5')); 36.317 (C<sub>endo</sub>(1'')); 36.168 (C<sub>exo</sub>(1'")); 31.198, 31.162, 29.053, 29.034, 28.828, 28.778, 28.583, 28.555, 23.503, 22.859, 21.984, 21.961 (13 x CH<sub>2</sub>(ketal)); 13.808, 13.787 (2 x Me). HR-ESI-MS: 533.35 g/mol [M+H]<sup>+</sup>; C<sub>29</sub>H<sub>48</sub>N<sub>4</sub>O<sub>5</sub> (532.36). Anal. calc. for C<sub>29</sub>H<sub>48</sub>N<sub>4</sub>O<sub>5</sub> (532.36 g/mol): C 65.38, H 9.08, N 10.52. Found: C 65.23, H 8.94, N 10.29.

**9-(6-Hydroxymethyl-2,2-dinonyl-tetrahydro-furo[3,4-d][1,3]dioxol-4-yl)-1-(3,7,1-trimethyl-dodeca-2,6,10-trienyl)-1,9-dihydro-purin-6-one (7, NL\_6.3.3.0).** TLC (SiO<sub>2</sub> 60, CH<sub>2</sub>Cl<sub>2</sub>/MeOH 97:3): R<sub>f</sub> 0.33. UV (MeOH): 250 (12.600). <sup>1</sup>H-NMR ((D<sub>6</sub>)DMSO): 8.327 (s, H-C(2)); 8.303 (s, H-C(8)); 6.097 (d, J(1',2') = 1.5, H-C(1')).

5.278 – 5.252 (*m*, H-C(2''), HO-C(5')); 5.032 – 4.977 (*m*, H-C(2'), H-C(6''), H-C(10)); 4.925 (*dd*,  $J(3',2') = 6.0$ ,  $J(3',4') = 1.5$ , H-C(3')); 4.616 (*d*,  $J(1'',2'') = 7.0$ , H-C(1'')); 4.213 – 4.188 (*m*, H-C(4')); 3.518 – 3.499 (*m*, CH<sub>2</sub>(5')); 2.048 (*t*,  $J(8'',9'') = 7.0$ , CH<sub>2</sub>(8'')); 1.997 (*t*,  $J(9'',8'') = 7.0$ , CH<sub>2</sub>(9'')); 1.929 (*t*,  $J(5'',4'') = 7.0$ , CH<sub>2</sub>(5'')); 1.859 (*t*,  $J(4'',5'') = 7.0$ , CH<sub>2</sub>(4'')); 1.780 (*s*, Me(13'')); 1.724 – 1.694 (*m*, CH<sub>2</sub>(1''<sub>endo</sub>)); 1.601 (*s*, Me(12'')); 1.560 – 1.539 (*m*, CH<sub>2</sub>(1''<sub>exo</sub>)); 1.517 (*s*, Me(14'')); 1.505 (*s*, Me(15'')); 1.290 – 1.225 (*m*, 14 x CH<sub>2</sub>(ketal)); 0.851, 0.835 (2 *s*, 2 x Me). <sup>13</sup>C-NMR ((D<sub>6</sub>)DMSO): 155.596 (C(6)); 147.989 (C(2)); 146.628 (C(4)); 140.133 (C(3'')); 139.164 (C(8)); 134.566 (C(7'')); 130.434 (C(11'')); 123.939 C(6''); 123.717 (C(5)); 123.340 (C(10'')); 119.270 C(2''); 116.667 (C(acetal)); 89.425 (C(4'')); 87.071 (C(1'')); 84.049 (C(2'')); 81.400 (C(3'')); 61.423 (C(5'')); 39.759 (C(4'')); 39.587 (C(8'")); 36.311 (C<sub>endo</sub>(1'")); 36.169 (C<sub>exo</sub>(1'")); 31.181, 31.142, 29.046, 29.031, 28.816, 28.763, 28.570, 28.539, 23.486, 22.843, 21.971, 21.945 (12 x CH<sub>2</sub>(ketal)); 26.064 (C(5'")); 25.602 (C(9'")); 25.283 (C(12'")); 17.307 (C(13'")); 16.089 (C(14'")); 15.660 (C(15'")); 13.777, 13.751 (2 x Me(ketal)). HR ESI MS: 737.88 [M+H]<sup>+</sup>; C<sub>44</sub>H<sub>72</sub>N<sub>4</sub>O<sub>5</sub> (737.07). Anal. calc. for C<sub>44</sub>H<sub>72</sub>N<sub>4</sub>O<sub>5</sub> (737.07): C 71.70, H 9.85, N 7.60. Found: C 71.64, H 9.70 N 7.68.

**Ethyl 3-{4-hydroxymethyl-2-methyl-6-[1-(3-methyl-but-2-enyl)-6-oxo-1,6-dihydro-purin-9-yl]-tetrahydro-furo[3,4-d][1,3]dioxol-2-yl}-propionate (8a, NL\_6.1.1.0, <sup>[23]</sup>).** TLC (SiO<sub>2</sub> 60, CH<sub>2</sub>Cl<sub>2</sub>/MeOH 9:1) R<sub>f</sub> 0.6. UV (MeOH): 251 (7.930). <sup>1</sup>H-NMR ((D<sub>6</sub>)DMSO); (1*R*)-diastereoisomer: 8.39 (*s*, H-C(2)); 8.29 (*s*, H-C(8)); 6.11 (*d*,  $J(1',2') = 2.5$ , H-C(1'')); 5.34 (*dd*,  $J(2',1') = 2.4$ ,  $J(2',3') = 6.5$ , H-C(2'')); 5.28 (*t*,  $J(2'',1'') = 7.3$ , H-C(2'')); 5.03 (*t*,  $J(HO-C(5'),CH_2(5')) = 5.2$ , HO-C(5')); 4.96 (*dd*,  $J(3',2') = 6.3$ ,  $J(3',4') = 2.5$ , H-C(3'')); 4.61 (*d*,  $J(1'',2'') = 7.3$ , CH<sub>2</sub>(1'')); 4.21 (*td*,  $J(4',3') = 2.5$ ,  $J(4',5') = 5.0$ , H-C(4'')); 4.08 (*q*,  $J(CH_2(\text{ester}),\text{Me}(\text{ester})) = 6.9$ ,

$\text{CH}_2(\text{ester})$ ); 3.50 (*td*,  $\text{CH}_2(5')$ ); 2.46 (*t*,  $^3J(\text{CH}_2(\text{C=O}), \text{CH}_2(\text{acetal})) = 7.6$ ,  $\text{CH}_2(\text{C=O})$ ); 2.08 (*t*,  $^3J(\text{CH}_2(\text{acetal}), \text{CH}_2(\text{C=O})) = 7.6$ ,  $\text{CH}_2(\text{acetal})$ ); 1.79 (*s*,  $\text{Me}(4'')$ ); 1.70 (*s*,  $\text{Me}(5'')$ ); 1.31 (*s*,  $\text{Me}(\text{acetal})$ ); 1.20 (*t*,  $^3J(\text{Me}(\text{ester}), \text{CH}_2(\text{ester})) = 7.1$ ,  $\text{CH}_2(\text{ester})$ ).  $^{13}\text{C}$ -NMR (( $\text{D}_6$ )DMSO); (*1R*)-diastereoisomer: 172.46 ( $\text{C=O}(\text{ester})$ ); 155.63 ( $\text{C}(6)$ ); 148.19 ( $\text{C}(2)$ ); 146.86 ( $\text{C}(4)$ ); 139.18 ( $\text{C}(3'')$ ); 136.67 ( $\text{C}(8)$ ); 123.79 ( $\text{C}(5)$ ); 119.46 ( $\text{C}(2'')$ ); 113.72 ( $\text{C}(\text{acetal})$ ); 89.29 ( $\text{C}(1')$ ); 86.80 ( $\text{C}(4')$ ); 83.79 ( $\text{C}(3')$ ); 81.15 ( $\text{C}(2')$ ); 61.31 ( $\text{C}(5'')$ ); 59.82 ( $\text{CH}_2(\text{ester})$ ); 43.36 ( $\text{C}(1'')$ ); 33.33 ( $\text{CH}_2(\text{C=O})$ ); 28.08 ( $\text{CH}_2(\text{acetal})$ ); 25.25 ( $\text{C}(4'')$ ); 23.44 ( $\text{Me}(\text{acetal})$ ); 17.82 ( $\text{C}(5'')$ ); 13.98 ( $\text{Me}(\text{ester})$ ). HR-ESI-MS: 485.27 [ $\text{M}+\text{Na}]^+$ ;  $\text{C}_{22}\text{H}_{30}\text{N}_4\text{O}_7$  (462.21). Anal. calc. for  $\text{C}_{22}\text{H}_{30}\text{N}_4\text{O}_7$  (462.50): C 57.13, H 6.54, N 12.11. Found: C 57.48, H 6.60, N 11.64.

**Ethyl 3-{4-[1-(3,7-Dimethyl-octa-2,6-dienyl)-6-oxo-1,6-dihydro-purin-9-yl]-6-hydroxymethyl- 2-methyl-tetrahydro-furo[3,4-d][1,3]dioxol-2-yl}-propionate (8b, NL\_6.1.12.0, [23]).** M.p. 100 °C. TLC ( $\text{SiO}_2$  60,  $\text{CH}_2\text{Cl}_2/\text{MeOH} = 95:5$ , v/v)  $R_f$  0.32. UV (MeOH): 246 (8.100).  $^1\text{H}$ -NMR (( $\text{D}_6$ )DMSO); (*1R*)-diastereoisomer: 8.366 (*s*,  $\text{H-C}(2)$ ); 8.290 (*s*,  $\text{H-C}(8)$ ); 6.111 (*d*,  $^3J(1',2') = 2.2$ ,  $\text{H-C}(1')$ ); 5.333 (*dd*,  $^3J(2',1') = 2.4$ ,  $^3J(2',3') = 6.1$ ,  $\text{H-C}(2')$ ); 5.271 (*t*,  $^3J(2'',1'') = 6.6$ ,  $\text{H-C}(2'')$ ); 5.028 (*m*, br.,  $\text{HO-C}(5')$ ,  $\text{H-C}(6'')$ ); 4.959 (*dd*,  $^3J(3',2') = 6.5$ ,  $^3J(3',4') = 2.4$ ,  $\text{H-C}(3')$ ); 4.614 (*d*,  $^3J(1'',2'') = 6.9$ ,  $\text{CH}_2(1'')$ ); 4.215 (*m*, br.,  $\text{H-C}(4')$ ); 4.08 (*q*,  $^3J(\text{CH}_2(\text{ester}), \text{Me}(\text{ester})) = 6.9$ ,  $\text{CH}_2(\text{ester})$ ); 3.503 (*s*, br.,  $\text{CH}_2(5')$ ); 2.458 (*t*,  $^3J(\text{CH}_2(\text{C=O})), \text{CH}_2(\text{acetal})) = 7.6$ ,  $\text{CH}_2(\text{C=O})$ ); 2.089 - 1.978 (3 *m*,  $\text{CH}_2(\text{acetal})$ ,  $\text{CH}_2(4''), \text{CH}_2(5'')$ ); 1.821 (*s*,  $\text{Me}(9'')$ ); 1.630 (*s*,  $\text{Me}(8'')$ ); 1.569 (*s*,  $\text{Me}(10'')$ ); 1.344 (*s*,  $\text{Me}(\text{acetal})$ ); 1.242 (*t*,  $^3J(\text{Me}(\text{ester}), \text{CH}_2(\text{ester})) = 7.0$ ,  $\text{Me}(\text{ester})$ ).  $^{13}\text{C}$ -NMR (( $\text{D}_6$ )DMSO); (*1R*)-diastereoisomer: 172.48 ( $\text{C=O}(\text{ester})$ ); 155.64 ( $\text{C}(6)$ ); 148.14 ( $\text{C}(2)$ ); 146.86 ( $\text{C}(4)$ ); 140.19 ( $\text{C}(3'')$ ); 139.18 ( $\text{C}(8)$ ); 130.95 ( $\text{C}(7'')$ ); 123.77 ( $\text{C}(6'')$ ); 123.64 ( $\text{C}(5)$ ); 119.26 ( $\text{C}(2'')$ ); 113.75 ( $\text{C-acetal}$ ); 89.28 ( $\text{C}(1')$ ); 86.76 ( $\text{C}(4')$ );

83.79 (C(2')); 81.17 (C(3')); 61.33 (C(5')); 59.83 (CH<sub>2</sub>(ester)); 43.21 (C(1'')); 38.79 (C(4'")); 33.34 (CH<sub>2</sub>(C=O); 28.09 (CH<sub>2</sub>(acetal)); 25.70 (C(5'")); 25.28 (C(8'")); 23.45 (Me(acetal); 17.42 (C(10'")); 16.13 (C(9'")); 13.99 (Me(ester)). HR-ESI-MS: 531.28 [M+H]<sup>+</sup>. C<sub>27</sub>H<sub>38</sub>N<sub>4</sub>O<sub>7</sub> (530.27). Anal. calc. for C<sub>27</sub>H<sub>38</sub>N<sub>4</sub>O<sub>7</sub> (530.27): C 61.12, H 7.22, N 10.56. Found: C 61.13, H 7.13, N 10.23.

**Ethyl 3-{4-hydroxymethyl-2-methyl-6-[6-oxo-1-(3,7,11-trimethyl-dodeca-2,6,10-trienyl)-1,6-dihydro-purin-9-yl]-tetrahydro-furo[3,4-d][1,3]dioxol-2-yl}propionate (8c, NL\_6.1.<sup>13.0</sup>, <sup>[23]</sup>)**. TLC (SiO<sub>2</sub> 60, CH<sub>2</sub>Cl<sub>2</sub>/MeOH 97:3): R<sub>f</sub> 0.13. UV (MeOH): 250 (15.300). <sup>1</sup>H-NMR ((D<sub>6</sub>)DMSO): 8.361 (s, H-C(2)); 8.292 (s, H-C(8)); 6.107 (s, H-C(1'')); 5.324 (*t*, <sup>3</sup>J(2'',1'') = 4.5, H-C(2'")); 5.274 (*t*, <sup>3</sup>J(HO-C(5'),CH<sub>2</sub>(5')) = 6.5, HO-C(5'')); 5.044 – 4.959 (*m*, CH<sub>2</sub>(1''), H-C(2'), H-C(3'')); 4.624, 4.611 (2s, H-C(6''), H-C(10'")); 4.216 (s, br, H-C(4'')); 4.084 (*q*, <sup>3</sup>J(CH<sub>2</sub>(ester),Me(ester)) = 7.0, CH<sub>2</sub>(ester)); 3.508 (*m*, CH<sub>2</sub>(5'')); 2.461 (*t*, <sup>3</sup>J(CH<sub>2</sub>(C=O),CH<sub>2</sub>(acetal)) = 7.5, CH<sub>2</sub>(C=O)); 2.091 – 1.857 (4 *m*, CH<sub>2</sub>(acetal), CH<sub>2</sub>(4''), CH<sub>2</sub>(5''), CH<sub>2</sub>(8''), CH<sub>2</sub>(9'")); 1.786 (s, Me(13'")); 1.609 (s, Me(14'")); 1.525, 1.516 (2 s, Me(15''), Me(12'")); 1.305 (s, Me(acetal)); 1.202 (*t*, <sup>3</sup>J(Me(ester),CH<sub>2</sub>(ester)) = 7.5, Me(ester)). <sup>13</sup>C-NMR ((D<sub>6</sub>)DMSO): 172.423 (C=O(ester)); 155.595 (C(6)); 148.085 (C(2)); 146.816 (C(4)); 140.115 (C(3'')); 139.112 (C(8)); 134.588 (C(7'")); 130.477 (C(11'")); 123.919 (C(6'")); 123.753 (C(5)); 123.360 (C(10'")); 119.238 (C(2'")); 113.713 (C(acetal)); 89.257 (C(4'")); 86.913 (C(1'')); 83.786 (C(2'")); 81.150 (C(3'")); 61.299 (C(5'")); 59.792 (CH<sub>2</sub>(ester)); 43.165 (C(1'")); 39.007 (C(8'")); 38.736 (C(4'")); 33.319 (CH<sub>2</sub>(C=O); 28.061 (CH<sub>2</sub>(acetal)); 26.015 (C(5'")); 25.537 (C(9'")); 25.300 (C(12'")); 23.402 (Me(acetal)); 17.340 (C(13'")); 16.114 (C(14'")); 15.674 (C(15'")); 13.953 (Me(ester)). HR-ESI-MS: 599.32

g/mol [M+H]<sup>+</sup>; C<sub>32</sub>H<sub>46</sub>N<sub>4</sub>O<sub>7</sub> (598.34). Anal. calc. for C<sub>32</sub>H<sub>46</sub>N<sub>4</sub>O<sub>7</sub> (598.73 g/mol): C 64.19, H 7.74, N 9.36. Found: C 64.20, H 7.54, N 8.98.

**Repetition of the Formerly Described Experiment at Elevated Temperature**

**Yielding 8c and 9-{[2,3-O[(1*R*)-4-Ethoxy-1-methyl-4-oxobutylidene]-β-D-ribofuranosyl}-6-[(2*E*,6*E*,9*E*,13*E*,17*E*)-3,7,11,11,14,18,22-heptamethyltricosa-2,6,9,13,17,21-hexaen-1-yl]oxy}-9*H*-purine (12, via non-isolated 8d).** TLC (SiO<sub>2</sub> 60, CH<sub>2</sub>Cl<sub>2</sub>/MeOH = 93:7, v/v): R<sub>f</sub>, 0.66. UV MeOH): λ<sub>max</sub> = 253 nm (ε = 15.400 mol<sup>-1</sup> cm<sup>-1</sup>); λ<sub>max</sub> = 269.5 nm (ε = 15.300 mol<sup>-1</sup> cm<sup>-1</sup>). The compound was identical with an authentic sample of compound **8c** in all other respects (<sup>1</sup>H-NMR, <sup>13</sup>C-NMR, HR ESI MS). From the slower migrating zone the title compound **12** was isolated as a colourless oil (115 mg, 0.142 mmol, 37.4 %). TLC (SiO<sub>2</sub> 60, CH<sub>2</sub>Cl<sub>2</sub>/MeOH = 93:7, v/v): R<sub>f</sub>, 0.49. UV (pH 3): λ<sub>max</sub> = 253 nm (ε = 9.200 mol<sup>-1</sup> cm<sup>-1</sup>). UV (pH 7): λ<sub>max</sub> = 224.5 nm (ε = 33.700 mol<sup>-1</sup> cm<sup>-1</sup>); λ<sub>max</sub> = 252.3 nm (ε = 6.000 mol<sup>-1</sup> cm<sup>-1</sup>). UV (pH 9): λ<sub>max</sub> = 224.5 nm (ε = 33.500 mol<sup>-1</sup> cm<sup>-1</sup>); λ<sub>max</sub> = 252.3 nm (ε = 5.900 mol<sup>-1</sup> cm<sup>-1</sup>). <sup>1</sup>H-NMR ((D<sub>6</sub>)DMSO): 9.719 (s, H-C(2)); 8.753 (s, H-C(8)); 8.239 (s, H-C(1')); 5.442 (t, <sup>3</sup>J(2'',1'') = 6.5, H-C(2'')); 5.336 (dd, <sup>3</sup>J(2',1') = 1.2, <sup>3</sup>J(2',3') = 6.0, H-C(2'')); 5.285 (t, <sup>3</sup>J(HO-C(5'),CH<sub>2</sub>(5')) = 6.5, HO-C(5')); 5.150 – 5.136 (m, 3H, CH<sub>2</sub>(1''), (=CH-)); 5.053 – 5.023 (m, 3H, (=CH-)); 4.693 - 4.679 (2m, H-C(6''), H-C(10'')); 4.563 – 4.550 (m, H-C(4')); 4.077 (q, <sup>3</sup>J(CH<sub>2</sub>(ester),Me(ester)) = 7.0, CH<sub>2</sub>(ester)); 3.687 – 3.600 (m, CH<sub>2</sub>(5')); 2.441 (t, <sup>3</sup>J(CH<sub>2</sub>(C=O),CH<sub>2</sub>(acetal)) = 7.5, CH<sub>2</sub>(C=O)); 2.104 – 1.877 (m, 18H, CH<sub>2</sub>(acetal), H-C(4''), H-C(5''), H-C(8''), H-C(12''), H-C(15''), H-C(16''), H-C(19''), H-C(20'')); 1.808, 1.796, 1.623, 1.539 (4s, 24H, 8 x Me); 1.314 (s, Me(acetal)); 1.195 (s, <sup>3</sup>J(Me(ester),CH<sub>2</sub>(ester)) = 7.5, Me(ester)). <sup>13</sup>C-NMR ((D<sub>6</sub>)DMSO), partly non-assigned and partly tentative assignments, indicated by an

asterisk (\*): 172.430 (C=O(ester)); 152.064 (C(2)); 151.782 (C(6)); 145.231 (C(4)); 143.534; 141.642 (C(3'')\*); 139.006 (C(8)); 134.773; 134.701 (C(7'')\*); 130.606 (C(11'')); 123.947 (C(6'')); 123.369 (C(5)); 123.275 (C(10'')); 117.844 C(2'')); 116.573; 114.031; 113.251 (C(acetal)); 93.657 (C(4')); 89.237 (C(1')); 84.672 (2''); 81.408 (C(3'')); 61.048 (C(5'')); 59.856 (CH<sub>2</sub>(ester)); 47.037; 44.256 (C(1'")); 39.663 (C(8'")); 38.818 (C(4'")); 33.112 (CH<sub>2</sub>(C=O)); 27.934 (CH<sub>2</sub>(acetal)); 26.121; 26.092 (C(5'")\*); 25.623 (C(9'")\*); 25.619 (C(12'")\*); 25.356; 23.304 (Me(acetal)); 17.418 (C(13'")\*); 16.400; 16.241 (C(14'")\*); 15.692 (Me(ester)). HR ESI MS: 803.87 g/mol [M+H]<sup>+</sup>; C<sub>47</sub>H<sub>70</sub>N<sub>4</sub>O<sub>7</sub> (803.08 g/mol).

**Prenylation of the Adenosine-O-2',3'-Ketal 3 – General Procedure.**

**6-Amino-9-[2-(2-ethoxycarbonyl-ethyl)-6-hydroxymethyl-2-methyl-tetrahydro-furo[3,4-d][1,3]dioxol-4-yl]-1-(3-methyl-but-2-enyl)-9H-purin-1-i um bromide (9a, NL\_5.1.1.0, [23]).** Yield: 0.44 g (0.95 mmol, 63%) of a white solid. M.p. 93°C. TLC (SiO<sub>2</sub> 60, CH<sub>2</sub>Cl<sub>2</sub>/MeOH 9:1): R<sub>f</sub> 0.2. UV (MeOH): 259 (10.670). <sup>1</sup>H-NMR [D<sub>6</sub>]DMSO); (1*R*) diastereoisomer: 9.27 (s, H<sub>2</sub>-N(6)); 8.56 (s, H-C(2)); 8.54 (s, H-C(8)); 6.16 (s, H-C(1'')); 5.35 – 5.37 (m, H-C(2'), H-C(2'")); 5.05 (*t*, <sup>3</sup>J(HO-C(5'),CH<sub>2</sub>(5')) = 5.2, HO-C(5'")); 4.98 (*d*, <sup>3</sup>J(3',2') = 6.6, H-C(3'")); 4.82 (*d*, <sup>3</sup>J(1'',2'") = 6.3, CH<sub>2</sub>(1'")); 4.28 (s, H-C(4'")); 4.09 (m, CH<sub>2</sub>(ester)); 3.52 (*t*, <sup>3</sup>J(HO-C(5'),CH<sub>2</sub>(5')) = 5.0, CH<sub>2</sub>(5'")); 2.46 (*t*, <sup>3</sup>J(CH<sub>2</sub>(C=O),CH<sub>2</sub>(acetal)) = 7.6, CH<sub>2</sub>(C=O)); 2.08 (*t*, <sup>3</sup>J(CH<sub>2</sub>(acetal),CH<sub>2</sub>(C=O)) = 7.4, CH<sub>2</sub>(acetal)); 1.79 (s, Me(4'")); 1.75 (s, Me(5'")); 1.31 (s, Me(acetal)); 1.20 (*t*, <sup>3</sup>J(Me(ester),CH<sub>2</sub>(ester)) = 7.1, Me(ester)). <sup>13</sup>C-NMR [D<sub>6</sub>]DMSO ); (1*R*) diastereoisomer: 172.46 (C=O(ester)); 150.74 (C(6)); 147.21 (C(2)); 141.64 (C(3'")); 139.20 (C(8)); 120.08 (C(5)); 116.70 (C(2'")); 113.70 (C(acetal)); 89.92 (C(1'")); 87.27 (C(4'")); 83.92 (2'")); 81.23 (C(3'")); 61.27 (C(5'")); 59.84 (CH<sub>2</sub>(ester)); 47.02 (C(1'"));

33.30 ( $\text{CH}_2(\text{C}=\text{O})$ ); 28.07 ( $\text{CH}_2(\text{acetal})$ ); 25.34 ( $\text{C}(4'')$ ); 23.43 ( $\text{Me}(\text{acetal})$ ); 18.09 ( $\text{C}(5'')$ ); 14.01 ( $\text{Me}(\text{ester})$ ). HR ESI MS: 463.31 [ $\text{M}+\text{H}]^+$ ;  $\text{C}_{22}\text{H}_{32}\text{N}_5\text{O}_6$  (462.21). Anal. calc. for  $\text{C}_{22}\text{H}_{32}\text{N}_5\text{O}_6 * 1.05 \text{CH}_2\text{Cl}_2$  (551.70): C 50.18, H 6.23, N 12.69. Found: C 50.04, H 6.04 N 13.14.

**6-Amino-1-(3,7-dimethyl-octa-2,6-dienyl)-9-[2-(2-ethoxycarbonyl-ethyl)-6-hydroxymethyl-2-methyl-tetrahydro-furo[3,4-d][1,3]dioxol-4-yl]-9H-purin-1-i um bromide (9b, NL\_5.1.12.0, [23]).** Yield: 0.78 g (1.48 mmol, 58%) of a slightly yellowish solid. M.p. 69°C. TLC ( $\text{SiO}_2$  60,  $\text{CH}_2\text{Cl}_2/\text{MeOH}$  9:1):  $R_f$  0.33. UV (MeOH): 261 (10.500).  $^1\text{H-NMR}$  ( $\text{D}_6$ )DMSO); ( $1R$ ) diastereoisomer: 9.31 (s,  $\text{H}_2(\text{N}(6))$ ); 8.56 (s,  $\text{H-C}(2)$ ); 8.50 (s,  $\text{H-C}(8)$ ); 6.12 ( $d$ ,  $^3J(1',2') = 2.2$ ,  $\text{H-C}(1')$ ); 5.34 – 5.38 ( $m$ ,  $\text{H-C}(2')$ ,  $\text{H-C}(2'')$ ); 5.03 – 5.11 ( $m$ ,  $\text{H-C}(3')$ ); 4.95 – 5.00 ( $m$ ,  $\text{H-C}(6'')$ ,  $\text{H-C}(10'')$ ,  $\text{CH}_2(1'')$ ); 4.82 ( $d$ ,  $^3J(\text{HO-C}(5'),\text{CH}_2(5')) = 6.9$ ,  $\text{HO-C}(5')$ ); 4.28 ( $m$ ,  $\text{H-C}(4')$ ); 4.08 ( $q$ ,  $^3J(\text{CH}_2(\text{ester}),\text{Me}(\text{ester})) = 6.9$ ,  $\text{CH}_2(\text{ester})$ ); 3.52 (s, br.,  $\text{CH}_2(5')$ ); 2.45 ( $t$ ,  $^3J(\text{CH}_2(\text{C}=\text{O}),\text{CH}_2(\text{acetal})) = 7.9$ ,  $\text{CH}_2(\text{C}=\text{O})$ ); 2.01 – 2.11 ( $m$ ,  $\text{CH}_2(5'')$ ,  $\text{CH}_2(1'')$ ,  $\text{CH}_2(4'')$ ); 1.78 (s,  $\text{Me}(\text{C}(9''))$ ); 1.61 (s,  $\text{Me}(8'')$ ); 1.53 (s,  $\text{Me}(10'')$ ); 1.31 (s,  $\text{Me}(\text{acetal})$ ); 1.20 ( $t$ ,  $^3J(\text{Me}(\text{ester}),\text{CH}_2(\text{ester})) = 7.1$ ,  $\text{Me}(\text{ester})$ ).  $^{13}\text{C-NMR}$  (( $\text{D}_6$ )DMSO); ( $1R$ ) diastereoisomer: 172.44 ( $\text{C}=\text{O}(\text{ester})$ ); 150.79 ( $\text{C}(6)$ ); 147.18 ( $\text{C}(2)$ ); 145.01 ( $\text{C}(4)$ ); 142.70 ( $\text{C}(3'')$ ); 141.60 ( $\text{C}(8)$ ); 131.43 ( $\text{C}(7'')$ ); 123.59 ( $\text{C}(5)$ ); 120.16 ( $\text{C}(6'')$ ); 116.49 ( $\text{C}(2'')$ ); 113.73 ( $\text{C}(\text{acetal})$ ); 89.93 ( $\text{C}(1')$ ); 87.21 ( $\text{C}(4')$ ); 83.92 ( $\text{C}(2')$ ); 81.23 ( $\text{C}(3')$ ); 61.29 ( $\text{C}(5')$ ); 59.87 ( $\text{CH}_2(\text{ester})$ ); 46.90 ( $\text{C}(1'')$ ); 38.83 ( $\text{C}(4'')$ ); 33.30 ( $\text{CH}_2(\text{C}=\text{O})$ ); 28.09 ( $\text{CH}_2(\text{acetal})$ ); 25.61 ( $\text{C}(5'')$ ); 25.32 ( $\text{C}(8'')$ ); 23.44 ( $\text{Me}(\text{acetal})$ ); 17.47 ( $\text{C}(10'')$ ); 16.42 ( $\text{C}(9'')$ ); 14.02 ( $\text{Me}(\text{ester})$ ). HR ESI MS: 531.61 [ $\text{M}+\text{H}]^+$ ;  $\text{C}_{27}\text{H}_{40}\text{N}_5\text{O}_6$  (530.64). Anal. calc. for  $\text{C}_{27}\text{H}_{40}\text{N}_5\text{O}_6 * 1.1 \text{CH}_2\text{Cl}_2$  (624.06): C 54.08, H 6.82, N 11.22. Found: C 54.08, H 6.62, N 11.33.

**6-Amino-9-[2-(2-ethoxycarbonyl-ethyl)-6-hydroxymethyl-2-methyl-tetrahydro-furo[3,4-d][1,3]dioxol-4-yl]-1-(3,7,11-trimethyl-dodeca-2,6,10-trienyl)-9H-purin-1-ium bromide (9c, NL\_5.1.13.0, [23]).** Yield: 0.98 g (1.64 mmol, 67%) of a slightly orange oil. TLC ( $\text{SiO}_2$  60,  $\text{CH}_2\text{Cl}_2/\text{MeOH}$  9:1):  $R_f$  0.29. UV (MeOH): 266 (10.000).  $^1\text{H}$ -NMR [ $\text{D}_6$ ]DMSO); ( $1R$ ) diastereoisomer: 9.30 (s, H<sub>2</sub>-N(6)); 8.58 (s, H-C(2)); 8.52 (s, H-C(8)); 6.16 (*d*,  $^3J(1',2') = 2.2$ , H-C(1')); 5.34 – 5.38 (*m*, H-C(2'), H-C(2'')); 5.03 – 5.06 (*m*, H-C(3')); 4.98 – 5.01 (*m*, H-(C6''), H-C(10''),  $\text{CH}_2(1'')$ ); 4.84 (*t*,  $^3J(\text{HO}-\text{C}(5'),\text{CH}_2(5') = 6.6$ , HO-C(5')); 4.28 (*dt*,  $^3J(4',5') = 4.7$ ,  $J(4',3') = 2.2$ , H-C(4')); 4.06 (*q*,  $^3J(\text{CH}_2(\text{ester}),\text{Me}(\text{ester})) = 7.2$ ,  $\text{CH}_2(\text{ester})$ ); 3.52 (*d*,  $^3J(\text{HO}-\text{C}(5'),\text{CH}_2(5') = 6.5$ ,  $\text{CH}_2(5')$ ); 2.46 (*t*,  $^3J(\text{CH}_2(\text{C=O}),\text{CH}_2(\text{acetal})) = 7.6$ ,  $\text{CH}_2(\text{C=O})$ ); 2.04 – 2.09 (*m*,  $\text{CH}_2(5'')$ ,  $\text{CH}_2(\text{acetal})$ ,  $\text{CH}_2(8'')$ ); 1.95 ( $\Psi$ quint,  $^3J(9'',8'') = 7.1$ ;  $^3J(9'',10'') = 7.1$ ;  $\text{CH}_2(9'')$ ); 1.86 – 1.89 (*m*,  $\text{CH}_2(4'')$ ); 1.77 (s, Me(13'')); 1.62 (s, Me(14'')); 1.54 (s, Me(15'')); 1.50 (s, Me(12'")); 1.31 (s, Me(acetal)); 1.20 (*t*,  $^3J(\text{Me}(\text{ester}),\text{CH}_2(\text{ester})) = 7.3$ , Me(ester)).  $^{13}\text{C}$ -NMR [ $\text{D}_6$ ]DMSO); ( $1R$ ) diastereoisomer: 172.45 (C=O(ester)); 150.72 (C(6)); 147.09 (C(2)); 145.09 (C(4)); 142.70 (C(3'')); 141.48 (C(8)); 134.77 (C(7'')); 130.67 (C(11'")); 123.93 (C(6'")); 123.33 (C(10'")); 120.00 (C(5)); 116.43 (C(2'")); 113.70 (C(acetal)); 89.90 (C(1')); 87.23 (C(4')); 83.95 (C(2')); 81.28 (C(3')); 61.26 (C(5')); 59.84 ( $\text{CH}_2(\text{ester})$ ); 47.01 (C(1'")); 39.01 (C(4'")); 38.79 (C(8'")); 33.30 ( $\text{CH}_2(\text{C=O})$ ); 28.08 ( $\text{CH}_2(\text{acetal})$ ); 26.08 (C(5'")); 25.52 (C(9'")); 25.35 (C(12'")); 23.43 (Me(acetal)); 17.40 (C(13'")); 16.48 (C(14'")); 15.73 (C(15'")); 14.00 (Me(ester)). HR-ESI-MS: 599.61 [M+H]<sup>+</sup>;  $\text{C}_{32}\text{H}_{48}\text{N}_5\text{O}_6$  (598.75). Anal. calc. for  $\text{C}_{32}\text{H}_{48}\text{N}_5\text{O}_6 * 1.6$   $\text{CH}_2\text{Cl}_2$  (734.64): C 54.93, H 7.02, N 9.53. Found: C 55.11, H 6.82, N 9.73.

### General Procedure for the Dimroth Rearrangements of Compounds 9a-c

Yielding 10a-c<sup>[16 17]</sup>.

**Ethyl 3-{4-hydroxymethyl-2-methyl-6-[6-(3-methyl-but-2-enylamino)-purin-9-yl]-tetrahydro-furo[3,4-d][1,3]dioxol-2-yl}-propionate (10a, NL\_5.1.<sup>6</sup>1.0).** TLC (SiO<sub>2</sub> 60, CH<sub>2</sub>Cl<sub>2</sub>/MeOH 9:1):  $R_f$  0.31. UV (MeOH): 268 (16.300). log $P_{OW}$  ( ALOGPS 3.01): 2.78 ± 0.74. <sup>1</sup>H-NMR [D<sub>6</sub>]DMSO); (1R)-diastereoisomer: 8.31 (s, H-C(2)); 8.22 (s, H-C(8)); 7.85 (s, H-N(6)); 6.14 (d, <sup>3</sup>J(1',2') = 2.8, H-C(1')); 5.42 (d, <sup>3</sup>J(2',1') = 3.8, H-C(2')); 5.31 (s, HO-C(5')); 5.11 (s, H-C(3')); 5.00 (d, <sup>3</sup>J(1",2") = 6.6, CH<sub>2</sub>(1")); 4.20 (s, H-C(4')); 4.09 (q, <sup>3</sup>J(CH<sub>2</sub>(ester),Me(ester)) 7.3, CH<sub>2</sub>(ester)); 3.50 (d, CH<sub>2</sub>(5'), <sup>3</sup>J(HO-(5'),CH<sub>2</sub>(5')) = 4.2, CH<sub>2</sub>(5')); 2.47 (s, CH<sub>2</sub>(C=O)); 2.08 (s, CH<sub>2</sub>(acetal)); 1.70 (s, Me(4")); 1.67 (s, Me(5")); 1.31 (s, Me(acetal)); 1.21 (t, <sup>3</sup>J(Me(ester),CH<sub>2</sub>(ester)) = 7.1, Me(ester)). <sup>13</sup>C-NMR ((D<sub>6</sub>)DMSO); (1R)-diastereoisomer: 172.53 (C=O); 154.31 (C(6)); 152.54 (C(2), C(4)); 148.07 (C(3")); 139.37 (C(8)); 133.20 (C(5)); 122.00 (C(2")); 113.73 (C-acetal); 89.37 (C(1)); 86.56 (C(4)); 83.36 (C(3)); 81.31 (C(2)); 61.44 (C(5)); 59.86 (CH<sub>2</sub>(ester)); 51.30 (CH<sub>2</sub>(acetal)); 33.44 (CH<sub>2</sub>(C=O)); 28.16 (C(1")); 25.31 (C(4")); 23.49 (Me-acetal); 17.78 (C(5")); 14.02 (Me(ester)). HR-ESI-MS: 462.36 [M+H]<sup>+</sup>; C<sub>22</sub>H<sub>31</sub>N<sub>5</sub>O<sub>6</sub> (461.51). Anal. calc. for C<sub>22</sub>H<sub>31</sub>N<sub>5</sub>O<sub>6</sub> · 0.1 CH<sub>2</sub>Cl<sub>2</sub> (470.00): C 56.48, H 6.69, N 14.90. Found: C 56.70, H 6.62, N 14.92.

**3-{4-[6-(3,7-Dimethyl-octa-2,6-dienylamino)-purin-9-yl]-6-hydroxymethyl-2-methyl-tetrahydro-furo[3,4-d][1,3]dioxol-2-yl}-propionsäureethylester (10b, NL\_5.1.<sup>6</sup>2.0, [23]).** TLC (SiO<sub>2</sub> 60, CH<sub>2</sub>Cl<sub>2</sub>/MeOH, 9:1):  $R_f$  0.90. UV (MeOH): 268 (16.150). log $P_{OW}$  ( ALOGPS 3.01): 3.62 ± 0.7. <sup>1</sup>H-NMR [D<sub>6</sub>]DMSO); (1R)-diastereoisomer: 8.31 (s, H-C(2)); 8.22 (s, H-C(8)); 7.83 (s, H-N(6)); 6.11 - 6.16 (m, H-C(1)); 5.41 (dd, <sup>3</sup>J(2',1') = 6.3, <sup>3</sup>J(2',3') = 6.3, H-C(2)); 5.28 - 5.35 (dt, <sup>3</sup>J(2",1") = 5.5, H-C(2")); 5.10 - 5.14 (td, <sup>3</sup>J(3',2') = 5.5, <sup>3</sup>J(3',4') = 5.5, H-C(3)); 5.03 - 5.08 (tt,

$^3J(6'',5'') = 7.0$ , H-C(6'')); 4.96 - 5.02 (*m*, CH<sub>2</sub>(1''), Me(10'')); 4.17 - 4.25 (*m*, H-C(4'')); 3.98 - 4.13 (*q*, CH<sub>2</sub>(ester), HO-C(5')),  $^3J(CH_2(\text{ester}), \text{Me}(\text{ester})) = 7.0$ , CH<sub>2</sub>(ester)); 3.44 - 3.59 (*dquint*, CH<sub>2</sub>(5')),  $^3J(\text{OH}-\text{C}(5'), \text{CH}_2(5')) = 5.0$ , CH<sub>2</sub>(5')); 2.44 - 2.49 (*m*, CH<sub>2</sub>(C=O)); 2.06 - 2.12 (*dt*,  $J(5'',4'') = 6.5$ , CH<sub>2</sub>(5'')); 2.00 - 2.05 (*t*,  $J(4'',5'') = 7.0$ , CH<sub>2</sub>(4'')); 1.88 - 1.99 (*m*, CH<sub>2</sub>(acetal)); 1.70 (*s*, Me(9'')); 1.59 (*s*, Me(8'')); 1.54 (*s*, Me(10'')); 1.31 (*s*, Me(acetal)); 1.20 (*t*,  $^3J(\text{Me}(\text{ester}), \text{CH}_2(\text{ester})) = 7.1$ , Me(ester)).  $^{13}\text{C}$ -NMR [D<sub>6</sub>]DMSO); (1*R*)-diastereoisomer: 172.57 (C=O); 154.77 (C(6)); 152.21 (C(2)); 145.93 (C(4)); 139.38 (C(3'')); 136.69 (C(8)); 130.76 (C(7'')); 123.91 (C(5)); 121.70 (C(6'')); 113.77 (C-acetal); 89.40 (C(1'')); 86.54 (C(4'')); 83.38 (C(3')); 81.33 (C(2')); 61.44 (C(5')); 59.89 (CH<sub>2</sub>(ester)); 51.33 (C(1'')); 38.98 (C(4'")); 33.47 (CH<sub>2</sub>C=O); 28.19 (CH<sub>2</sub>(acetal)); 25.93 (C(5'")); 25.37 (C(8'")); 23.50 (Me(acetal)); 17.48 (C(10'")); 16.12 (C(9'")); 14.04 (Me(ester)). HR-ESI-MS: 530.36 [M+H]<sup>+</sup>; C<sub>27</sub>H<sub>39</sub>N<sub>5</sub>O<sub>6</sub> (529.63). Anal. calc. for C<sub>27</sub>H<sub>39</sub>N<sub>5</sub>O<sub>6</sub> · 0.7 DMF (546.55): C 60.87, H 7.49, N 13.40. Found: C 60.60, H 7.36, N 13.19.

**Ethyl 3-{4-Hydroxymethyl-2-methyl-6-[6-(3,7,11-trimethyl-dodeca-2,6,10-trienylamino)-purin-9-yl]-tetrahydro-furo[3,4-d][1,3]dioxol-2-yl}-propionate (10c, NL\_5.1.<sup>6</sup>3.0,<sup>[23]</sup>)**. TLC (SiO<sub>2</sub> 60, CH<sub>2</sub>Cl<sub>2</sub>/MeOH 9:1):  $R_f$  0.93. UV (MeOH): 267 (12.100). logP<sub>OW</sub> ( ALOGPS 3.01): 4.13 ± 0.74.  $^1\text{H}$ -NMR [D<sub>6</sub>]DMSO); (1*R*)-diastereoisomer: 8.31 (*s*, H-C(2)); 8.22 (*s*, H-C(8)); 7.83 (*s*, H-N(6)); 6.14 (*d*,  $^3J(1',2') = 2.8$ , H-C(1'')); 5.41 (*d*,  $^3J(2',1') = 4.1$ , H-C(2'')); 5.32 (*s*, H-C(2'')); 5.13 (*s*, H-C(3')); 5.06 (*d*,  $^3J(10'',9'') = 0.9$ , H-C(10'')); 4.98 - 5.01 (*m*, CH<sub>2</sub>(1''), H-C(6'')); 4.21 (*d*,  $^3J(4',3') = 2.5$ , H-C(4'')); 4.09 (*q*, CH<sub>2</sub>(ester), HO-C(5')),  $^3J(\text{CH}_2(\text{ester}), \text{Me}(\text{ester})) = 7.3$ , CH<sub>2</sub>(ester)); 3.45 - 3.58 (*m*, CH<sub>2</sub>(5'')); 2.45 - 2.48 (*m*, CH<sub>2</sub>(C=O)); 2.01 - 2.12 (*m*, CH<sub>2</sub>(8''), CH<sub>2</sub>(5''), CH<sub>2</sub>(acetal)); 1.94 - 2.00 (*m*, CH<sub>2</sub>C(9'')); 1.89 (*t*,  $^3J(4'',5'') = 8.2$ , CH<sub>2</sub>(4'')); 1.70 (*s*, Me(13'')); 1.61 (*s*, Me(14'')); 1.53 (*s*, Me(15'')); 1.52 (*s*, Me(12'')).

1.31 (s, Me(acetal); 1.20 (*t*,  $^3J(\text{Me(ester)}, \text{CH}_2(\text{ester})) = 7.1$ , Me(ester)).  $^{13}\text{C}$ -NMR [D<sub>6</sub>]DMSO); (1*R*)-diastereoisomer: 172.51 (C=O); 154.32 (C(6)); 152.50 (C(2)); 145.13 (C(4)); 139.32 (C(3"")); 136.61 (C(8)); 134.39 (C(7"")); 130.50 (C(11"")); 124.01 (C(6"")); 123.68 (C(10"")); 121.71 (C(5)); 119.46 (C(2"")); 113.73 (C-acetal); 89.39 (C(1'')); 86.54 (C(4'")); 83.36 (C(3'")); 81.32 (C(2'")); 61.44 (C(5'")); 59.84 (CH<sub>2</sub>(ester)); 51.27 (C(1"")); 39.01 (C(4"")); 38.92 (C(8"")); 33.44 (CH<sub>2</sub>(C=O)); 28.16 (CH<sub>2</sub>(acetal)); 26.09 (C(5"")); 25.79 (C(9"")); 25.34 (C(12"")); 23.46 (Me(acetal); 17.39 (C(13"")); 16.09 (C(14"")); 15.69 (C(15"")); 13.99 (Me(ester)). HR-ESI-MS: 598.44 [M+H]<sup>+</sup>; C<sub>32</sub>H<sub>47</sub>BrN<sub>5</sub>O<sub>6</sub> (597.75). Anal. calc. for C<sub>32</sub>H<sub>47</sub>BrN<sub>5</sub>O<sub>6</sub> (677.65): C 56.72, H 6.95, N 10.33. Found: C 56.64, H 6.96, N 10.23.